UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/733,212 | 12/11/2003 | Donald W. Kufe | GENU:009USD1/10717456 | 7998 |

32425 7590 03/02/2009

FULBRIGHT & JAWORSKI L.L.P.
600 CONGRESS AVE.
SUITE 2400
AUSTIN, TX 78701

| EXAMINER | |
|---|---|
| HILL, KEVIN KAI | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1633 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 03/02/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/733,212 | KUFE, DONALD W. | |
| | Examiner | Art Unit | |
| | KEVIN K. HILL | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-17,19 and 22-27* is/are pending in the application.

4a) Of the above claim(s) *2-4,6,10-12 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,7-9,13,15-17,19 and 22-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *October 22, 2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## Detailed Action

### *Election/Restrictions*

Applicant has elected without traverse the invention of Group I, claims 1-8, drawn to a method of identifying a compound that inhibits binding of MUC1 to a tumor progressor.

Applicant elected the tumor progressor species β-catenin (claim 5).

### *Amendments*

Applicant submitted an amendment, filed December 12, 2007, in response to the Final Office Action mailed June 12, 2007, and a Request for Continued Examination was filed concurrently. In response to these papers, a Non-Final Office Action was mailed March 3, 2008.

Applicant submitted a supplemental amendment, filed March 14, 2008, in response to the Final Office Action mailed June 12, 2007, in which Applicant withdrew Claims 2-4, 6, 10-12 and 14, amended Claims 1, 9, 13 and 18, and entered new claims, Claims 19-27. Because the amendment filed March 14, 2008 was a Non-Compliant Amendment to the Non-Final Office Action mailed March 3, 2008 (see Office Action mailed October 28, 2008), the new limitations to the claims, now entered, have not been previously examined.

Applicant submitted a supplemental amendment filed November 21, 2008 in response to the Notice of Non-Compliant Amendment mailed October 28, 2008, in which Applicant cancelled Claims 18 and 20-21, withdrew Claims 2-4, 6, 10-12 and 14, and amended Claims 1, 9 and 25.

Applicant's amendments have necessitated the new ground(s) of rejection presented in this Office action.

Claims 2-4, 6, 10-12 and 14 are pending but withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim.

Claims 1, 5, 7-9, 13, 15-17, 19 and 22-27 are under consideration.

### *Priority*

Applicant's claim for priority under 35 U.S.C. 119(e) or 120 regarding the parent provisional application 60/257,590, filed on December 22, 2000 and provisional application 60/308,307, filed on July 27, 2001 is acknowledged.

The effective priority date of the instant application is granted as December 22, 2000.

## *Information Disclosure Statement*

Applicant has filed Information Disclosure Statements on October 22, 2008, providing more than 315 references. The Examiner was able to consider these to the extent of time allowable. The signed and initialed PTO Forms 1449 are mailed with this action.

## *Examiner's Note*

Unless otherwise indicated, previous objections/rejections that have been rendered moot in view of the amendment will not be reiterated. The arguments in the November 21, 2008 response will be addressed to the extent that they apply to current rejection(s).

## *Claim Objections*

1. **Claims 13 and 26 are objected to because of the following informalities**:

With respect to Claim 13, the claim recites that the MUC1 test agent is phosphorylated. However, independent Claim 1, from which Claim 13 depends, recites that the MUC1 test agent is phosphorylated at the YEKV site. Thus, the recitation in Claim 13 is redundant, unnecessary and fails to further limit the status of the MUC1 test agent already phosphorylated at the YEKV site.

With respect to Claim 26, the term "PDCδ" is misspelled. See Claim 6 and specification (pg 1, line 14).

Appropriate correction is required.

## *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. **Claim 13 is rejected under 35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

the invention. The claim recites that the MUC1 test agent is phosphorylated. The metes and bounds of the claim is unclear because MUC1 comprises a plurality of serine, threonine and tyrosine residues capable of being phosphorylated and the instant claim does not disclose which residue(s) are to be phosphorylated in addition to the phosphorylated YEKV site (Claim 1). Stated another way, it is unclear if Applicant is claiming that the MUC1 test agent of Claim 13 must be phosphorylated at a site other than the YEKV site of Claim 1 or simply re-stating the phosphorylation of said YEKV site.

Appropriate correction is required.

## *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. **Claims 25-26 are rejected under 35 U.S.C. 112, first paragraph,** because the specification, while being enabling for a method of identifying a compound that inhibits binding of MUC1 to a tumor progressor, the method comprising ATP as a source of phosphate ions, does not reasonably provide enablement for an enormous genus of structurally distinct phosphate ion sources. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention. If not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence

of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue" (*In re Wands*, 858 F.2d 731, 737, 8 USPQ2ds 1400, 1404 (Fed. Cir. 1988)). Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification. Therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention. And thus, skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

***The Breadth of the Claims and The Nature of the Invention***

The breadth of the claims reasonably embrace *in vitro* kinase assays and reasonably encompass phosphate ion sources such as nucleotide monophosphates, nucleotide diphosphates, inorganic phosphates, and guanosine tri-, tetra- or penta-phosphate.

The inventive concept in the instant application is providing the Src and EGFR protein tyrosine kinases, and the PKCδ protein serine/threonine kinase with the phosphate ion source ATP that is recognized by the ATP-binding site said protein kinases.

***The Existence of Working Examples and The Amount of Direction Provided by the Inventor***

The specification discloses that Src, EGF-R and PKCδ can phosphorylate the cytoplasmic domain of MUC1 (pg 1, line 14). The specification teaches that the real world embodiment of the phosphate ion source is ATP (e.g. pg 24, line 27). The specification fails to disclose other phosphate ion sources to be used in the asserted inventive method from which the Src, EGF-R and PKCδ protein kinases may then phosphorylate the MUC1 target test agent.

***The State of the Prior Art, The Level of One of Ordinary Skill and The Level of Predictability in the Art***

The art teaches that protein serine, threonine and protein kinases recognize nucleotide triphosphates, specifically ATP, as the donor source of phosphate ions, from which the protein kinase may then transfer a phosphate ion onto its appropriate substrate amino acid. Hanks et al (FASEB J. 9:576-596, 1995) teach that protein kinases use the γ-phosphate of ATP to generate phosphate monoesters using protein alcohol groups on serine or threonine and/or protein

phenolic groups on tyrosine as phosphate acceptors (pg 576, col. 2). Src and EGF-R are known protein tyrosine kinases that use ATP as the source of phosphate ions. PCKδ is a known protein serine/threonine kinase that uses ATP as the source of phosphate ions. The prior art does not teach that the protein kinases of the invention are capable of using nucleotide monophosphates, nucleotide diphosphates, inorganic phosphate, nor guanosine tri-, tetra- or penta-phosphate as a source of phosphate ions.

***The Quantity of Any Necessary Experimentation to Make or Use the Invention***

Thus, the quantity of necessary experimentation to make or use the invention as claimed, based upon what is known in the art and what has been disclosed in the specification, will create an undue burden for a person of ordinary skill in the art to demonstrate that nucleotide monophosphates, nucleotide diphosphates, inorganic phosphate, guanosine tri-, tetra- or penta-phosphate may be used as a source of phosphate ions by the tumor progressor test agent to phosphorylate the MUC1 test agent.

In conclusion, the specification fails to provide any guidance as to how an artisan would have dealt with the art-recognized limitations of the claimed method commensurate with the scope of the claimed invention and therefore, limiting the claimed invention to a method of identifying a compound that inhibits binding of MUC1 to a tumor progressor, the method comprising ATP as a source of phosphate ions, is proper.

## *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. **The prior rejection of Claims 1, 5, 7-9, 13 and 15-18 under 35 U.S.C. 103(a)** as being unpatentable over Brent et al (U.S. Patent No. 6,004,746; *of record) in view of Li et al (Mol. Cell Biol. 18(12): 7216-7224, 1998, * of record in IDS), Yamamoto et al (J. Biol. Chem. 272(19): 12492-12494, 1997; *of record), and Zrihan-Licht et al (FEBS Letters 356(1):130-136, 1994) **is withdrawn** in light of Applicant's amendment to the claims.

5. **Claims 1, 5, 7-9, 13, 15-17 and 22-27 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Li et al (Mol. Cell Biol. 18(12): 7216-7224, 1998, *of record in IDS) in view of Yamamoto et al (J. Biol. Chem. 272(19): 12492-12494, 1997; *of record) and Barker et al (U.S. Patent 5,851,775), as evidenced by Li et al (J. Biol. Chem. 276(38):35239-35242, 2001; *of record in IDS) and Zrihan-Licht et al (FEBS Letters 356(1):130-136, 1994; *of record).

***Determining the scope and contents of the prior art.***

Li et al teach a method of identifying a compound that inhibits binding of the β-catenin tumor progressor to a MUC1 test agent, the method comprising the step of providing a MUC1 test agent comprising a YEKV site, providing a β-catenin test agent that binds to the MUC1 test agent, and contacting the MUC1 test agent with a test compound that is GSK-3β, wherein the GSK-3β test compound inhibits the binding of MUC1 to β-catenin, wherein the method is performed *in vitro* or in a cell, e.g. a cancer cell (pg 7220, Figure 4, Figure 5). Li et al teach the isolation the MUC1 test agent from human breast carcinoma cells for *in vitro* assays (pgs 7216-7217, joining ¶). Li et al taught that test compound GSK-3β binds directly to an STDRSPYE site of SEQ ID NO:1 in the cytoplasmic domain of the human MUC1 (see pg 7218, Figure 2), wherein amino acids YE are the first two amino acids of the YEKV site (SEQ ID NO:11). Phosphorylation of MUC1 by GSK-3β decreases binding of MUC1 to β-catenin *in vitro* and *in vivo*. Li et al taught that signals other than GSK-3β-mediated phosphorylation may contribute to regulation of the MUC1-β-catenin complex (pg 7222, col. 1). The site in MUC1 for GSK-3β binding and phosphorylation is adjacent and joined to the β-catenin binding site by the YEKV motif (Figure 2A). Li et al suggest that the association of GSK-3β with MUC1 may displace β-

catenin, and teach that GSK-3β inhibits the association of MUC1 and β-catenin *in vitro* and *in vivo* (pg 7222, col. 1). Li et al taught the use of a peptide aptamer to block the interaction between a MUC1 test agent and a GSK-3β test agent (pg 7218, Figure 2C), as well as the step of determining whether the MUC1 test agent is phosphorylated at a specific amino acid site (pg 7219, Figure 3).

Similarly, Yamamoto et al taught a method of identifying a compound that inhibits binding of the β-catenin tumor progressor to a MUC1 test agent, the method comprising providing a MUC1 test agent comprising a YEKV site (SEQ ID NO:11), providing a β-catenin tumor progressor test agent, contacting the MUC1 test agent with the β-catenin test agent in the presence of a test compound, wherein the contacting occurs *in vitro*, and determining whether the test compound inhibits binding of MUC1 to β-catenin (pg 12493, Figure 4). Yamamoto et al teach the isolation the MUC1 test agent from human breast carcinoma cells for *in vitro* assays (pg 12492, col. 1, Materials and Methods; pg 12493, Figure 1).

Neither Li et al nor Yamamoto et al teach the β-catenin test agent is a peptide fragment. However, at the time of the invention, Barker et al disclosed a method of identifying a compound that inhibits the binding of β-catenin to a protein with which β-catenin interacts, the method comprising contacting a test compound with a β-catenin test agent and a second test agent, and determining whether the test compound inhibits the binding of β-catenin to the second test agent (col. 2, lines 49-55). Assays for β-catenin inhibitors may be performed *in vitro* or in cells, for example, using a two-hybrid assay (col. 6, lines 51-54), wherein the cells may be cancer cells, e.g. colorectal, brain, breast or bone cancer cells. The first and second test agent may be introduced into the host cell (col. 3, lines 51-52; col. 4, lines 31-42; col. 6, line 60-col. 7, line 23), or may exist endogenously in the host cell, e.g. a colon carcinoma cell, such that the interaction between the first and second test agents exists endogenously in the host cell. The test compound may titrate β-catenin (col. 7, lines 16-18). Upon exposure to test compound, the binding between β-catenin and the second test agent is diminished (col. 9, lines 17-30). Barker et al disclose the test compound may be a fragment of β-catenin (col. 5, lines 6-35; col. 12, Example 8), wherein the instant specification discloses that the term "fragment" reasonably encompasses polypeptides "shorter than the full-length tumor progressor" (pg 4, lines 15-16).

***Ascertaining the differences between the prior art and the claims at issue.***

Neither Li et al, Yamamoto et al nor Barker et al teach *ipsis verbis* that the MUC1 test agent comprises a phosphorylated YEKV site. However, Zrihan-Licht et al taught that the cytoplasmic domain of MUC1 comprising SEQ ID NO:1 is extensively phosphorylated on tyrosine residues, wherein the art recognizes that phosphorylation on tyrosine residues is a key step in signal transduction pathways mediated by membrane proteins, e.g. MUC1. Zrihan-Licht et al demonstrate the ability to detect tyrosine phosphorylation of a MUC1 test agent (Zrihan-Licht et al, pg 132, Figure 1). Those of ordinary skill in the art were skilled in methods to determine whether a substrate is or is not phosphorylated. Furthermore, Li et al (2001) teach that in cancer cells, e.g. breast carcinoma cells, MUC1 associates constitutively with the epidermal growth factor receptor (EGF-R) which phosphorylates MUC1 at the YEKV site. Thus, in human cancers (Li, 1998; Yamamoto, Barker) which express MUC1 the endogenous MUC1 test agent will necessarily be phosphorylated at the YEKV site as part of the natural cell biology and metabolism of the cancer cells.

***Resolving the level of ordinary skill in the pertinent art.***

People of the ordinary skill in the art will be highly educated individuals including medical doctors, scientists, or engineers possessing advanced degrees such as M.D.'s and Ph.D.'s. Thus, these people most likely will be knowledgeable and well-read in the relevant literature and have the practical experience in molecular biology, biochemistry, and signal transduction. Therefore, the level of ordinary skill in this art is high.

At the time of the invention, the ordinary artisan knew and practiced methods to detect and identify protein-protein interaction domains, antagonists thereof, and how to determine whether or not a specific amino acid motif is phosphorylated, e.g. tyrosine phosphorylation, under a given condition.

***Considering objective evidence present in the application indicating obviousness or nonobviousness.***

It would have been obvious to one of ordinary skill in the art to substitute a first test compound with a test compound that is a peptide fragment of the tumor progressor β-catenin with a reasonable expectation of success because the simple substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention, the motivation being that Barker et al teach that the test compound that is a peptide fragment may be used to titrate non-mutant tumor progressor away from forming a protein complex [binding] with a test agent, and successfully demonstrate the utility of the tumor progressor peptide fragment in assays to validate the inhibition of binding between the tumor progressor and the test agent. Thus, the knowledge to design an appropriate screening system comprising the use of a peptide fragment of a test agent as a test compound was generally available to one of ordinary skill in the art at the time of the invention.

It also would have been obvious to one of ordinary skill in the art to try a MUC1 test agent comprising a phosphorylated YEKV site in a method to identify a compound that inhibits the binding between a tumor progressor test agent such as β-catenin and a MUC1 test agent because "a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipate success, it is likely that product not of innovation but of ordinary skill and common sense." An artisan would be motivated to try a MUC1 test agent comprising a phosphorylated YEKV site in a method to identify a compound that inhibits the binding between a tumor progressor test agent such as β-catenin and a MUC1 test agent because, at the time of the invention, those of ordinary skill in the art were already aware that:

i) the cytoplasmic domain of MUC1 comprising SEQ ID NO:1 is extensively phosphorylated on tyrosine residues,

ii) phosphorylation on tyrosine residues is a key step in signal transduction pathways mediated by membrane proteins, e.g. MUC1,

iii) there are but seven, immediately envisioned, tyrosines in the MUC1 cytoplasmic domain capable of being phosphorylated,

iii) the MUC1 cytoplasmic domain possessed a peptide motif that mediates binding to β-catenin,

iv) the YEKV (SEQ ID NO:11 within SEQ ID NO:1) peptide motif is immediately adjacent to the MUC1 peptide motif to which β-catenin binds, and

v) Yamamoto et al teach that "Whereas the cytoplasmic domain of MUC1 is phosphorylated on tyrosine, it is not known if tyrosine sites influence binding of catenins to the serine-rich motif." (pg 12494, col. 1). Thus, Yamamoto et al suggest the phosphorylation of one or more of the seven tyrosine residues in the MUC1 cytoplasmic domain to pursue this possible regulatory feature, wherein the YEKV site is immediately adjacent to the serine-rich motif.

The YEKV peptide motif (SEQ ID NO:11 within SEQ ID NO:1) is situated at a location that one of ordinary skill in the art would reasonably expect to affect the binding of one or more MUC1-interacting proteins, e.g. β-catenin, and there are only three possible outcomes regarding the effects of the YEKV peptide motif phosphorylation status:

1) tyrosine phosphorylation at YEKV promotes β-catenin binding to MUC1,

2) tyrosine phosphorylation at YEKV inhibits β-catenin binding to MUC1, and

3) tyrosine phosphorylation at YEKV has no effect for β-catenin binding to MUC1.

Thus, absent evidence to the contrary, the invention as a whole is *prima facie* obvious.

## ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned

with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. **Claims 1, 5, 7-9, 13 and 15-17 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting** as being unpatentable over claims 1, 5 and 7-8 of copending Application No. 10/032,786 (U.S. 2002/0110841 A1). Although the conflicting claims are not identical, they are not patentably distinct from each other because the method in the co-pending application comprises the use of a MUC1 test agent that possesses SEQ ID NO:1 and SEQ ID NO:11 of the instant application, the tumor progressor agent is β-catenin, and wherein the assay measures an inhibition of phosphorylation of MUC1 so as to inhibit binding of MUC1 to β-catenin [0152, Example 5]. Thus, the method in the co-pending application reasonably embraces and is substantially similar to the method claimed in the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Response to Amendment***

Applicants have indicated that they will deal with this rejection after the present claims are deemed otherwise allowable. However, it is noted that the absence of substantive arguments against the double patenting rejection(s) and/or acknowledgment regarding the intention of filing a terminal disclaimer is not sufficient. The rejection can not be held in abeyance, and it is maintained for the reasons of record until the aforementioned issues are resolved.

## *Conclusion*

7. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Kevin K. Hill, Ph.D. whose telephone number is 571-272-8036. The Examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kevin K. Hill/
Examiner, Art Unit 1633

/Q. JANICE LI, M.D./
Primary Examiner, Art Unit 1633